IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	: NAPARSTEK, Yaakov
Serial No.	: 09/826,069
Filed	: April 4, 2001
For	: PEPTIDES FOR THE TREATMENT OF : SYSTEMIC LUPUS ERYTHEMATOSUS : AND METHODS OF TREATING : SYSTEMIC LUPUS ERYTHEMATOSUS : : Group Art Unit 1644 : Examiner: G. EWOLDT

Hon. Commissioner of Patents and Trademarks
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DECLARATION UNDER 37 CFR SEC 1.132

I, the undersigned, Yaakov Naparstek, of 17 Davidson St., Jerusalem, Israel, hereby declare as follows:

1. Previous methods of treating systemic lupus erythematosus (SLE) include plasmapheresis, which has been used since 1974. In plasmapheresis a patient's plasma is separated from the blood cells and either discarded and replaced with substitute donor plasma or filtered with standard equipment and returned to the patient. All immune complexes and antibodies are thus removed from a patient's blood.

It is well known that treatment of patients with plasmapheresis must be followed by cyclophosphamide, for example, or other immunosuppressive drugs due to the rebound effect, in which the body compensates for the removal of antibodies by producing an overabundance of antibodies, leading to other deleterious side effects.

See, e.g., the enclosed articles, both of which document the rebound effect:

1. "Plasmapheresis: an adjunct therapy in severe progressive neuropsychiatric lupus.", *J. Assoc. Physicians India*, 2001 Oct; 49:986-9; and
2. "Immunoadsorption therapy (Therasorb) in patients with severe lupus erythematosus", *Acta Med. Austriaca*, 2002;29:26-29. Numerous other articles available on the internet document the rebound effect. Thus, plasmapheresis is only a moderately successful treatment for SLE at best, and in fact in several studies it has been shown to be no better than treatment with cyclophosphamide alone (see footnotes 17, 18 and 19 in Reference 2).

2. A newer therapy, described in Reference 2 above, is a type of immunoadsorption, in which a patient's blood is removed from the body and passed through a column which contains antibodies (such as sheep antibodies) which will bind human antibodies and remove them from the blood. Again, the removal is non-specific, i.e., all antibodies are removed, and there is concern about the rebound effect. In the study described in Reference 2, intravenous immunoglobulin was administered to the patients to avoid the rebound effect (see page 27, top paragraph of the right hand column). This therapy also has other disadvantages, such as the fact that the blood must be passed through the column numerous times (18 cycles) in order to accomplish a significant removal of antibodies.

The Gaubitz article, J. Autoimmunity (1998) 11, 495-501, cited as prior art by the Examiner in the captioned application, describes a comparison of the Therasorb column with another type of immunoadsorption column. The article does not discuss a rebound effect, but this could be due to concomitant immunosuppressive therapy (see table 2 and p. 500, left column, bottom paragraph).

3. In the present invention, extracorporeal removal of only lupus-specific antibodies from the plasma of SLE patients is accomplished by means of an adsorption column containing the R38 laminin peptide. This peptide specifically binds lupus antibodies and removes them from the plasma of a patient. In contrast to the other treatment methods described above, no rebound effect was observed in the patient data referred to in connection with the last declaration. A graph showing antibody levels in two patients pre- and one month post-treatment by methods of the present invention was inadvertently omitted with the last declaration, and it is included herewith. One of the patients did not receive any immunosuppressive treatment, while the other one received only low doses of corticosteroids and azathiorpine at the time of treatment with the methods of the present invention.

4. It is my well-considered opinion that the present invention is not obvious in view of any of the cited references, alone or in combination. It was completely unpredictable, and completely unexpected, that the present invention would work as described and overcome the obstacles and deleterious side effects shown in prior art treatment methods for SLE.

5. I declare that all the statements made herein of my own knowledge are true, and that all statements made on information and knowledge are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this 10 day of December 2007.

Yaakov Naparstek

Figure 1

Anti VRT level- before and one month after apheresis on the Lupusorb column